

the experiments here described monkeys have been used as subjects; the experiments were intended primarily to define specific problems so that the more expensive chimpanzee material might subsequently be used to better advantage. I am indebted to Professor Yerkes for his interest and effective support of these studies.

The present experiments very largely owe their inception to the work of Professor K. S. Lashley, who recognized the need for testing theories of cortical function in an animal form more closely resembling man than the rat. Mere citation of reference does not indicate the extent to which I have drawn upon his experimental work in the development of these problems. The debt to Professor J. F. Fulton is more direct. Not only did he make available the facilities of the Laboratory of Physiology, but he has enthusiastically participated in the physiological and surgical aspects of the studies. The clear-cut nature of the findings is, in no small measure, an expression of his surgical skill in producing circumscribed lesions of the cortex. Thanks are due also to Doctor Margaret A. Kennard for assistance on physiological and surgical aspects of the problem. Doctors D. G. Marquis and H. W. Nissen have read parts of the manuscript and have helpfully discussed and criticized various phases of the investigations.

These investigations have been aided by grants from the Research Funds of Yale University School of Medicine and by a grant from the Rockefeller Foundation to the Laboratory of Physiology.

C. F. J.

Vol. 13. pp 1-60. I. The functions  
of the frontal association areas in monkeys.  
Williams and Welkins, Baltimore. 1936.

## STUDIES OF CEREBRAL FUNCTION IN PRIMATES

C. F. JACOBSEN

WITH THE COÖPERATION OF J. H. ELDER AND G. M. HASLERUD

*From Yale Laboratories of Primate Biology*

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### FOREWORD

The three papers presented in this monograph constitute the first extensive report of a series of behavioral experiments on cerebral function in primates. They have been carried out as part of the program of the Yale Laboratories of Primate Biology. In

character and behavior, though it is difficult to state in precise terms the nature of the change. The animals operated on were selected on account of their intelligent character. After operation though they might seem to one who had not compared their present with their past, fairly up to the average of monkey intelligence, they had undergone a considerable psychological alteration. Instead of, as before, being actively interested in their surroundings, and curiously prying into all things that came within the field of their observation, they remained apathetic or dull, or dozed off to sleep, responding only to the sensations or impressions of the moment, or varying their listlessness with restlessness and purposive wanderings to and fro. While not actually deprived of intelligence, they had lost, to all appearance, the faculty of attentive and intelligent observation" (Ferrier (14), pp. 231-232).

Ferrier thus summarized his early observations on the effects of experimentally removing the frontal lobes in monkeys, and added impetus to the growing belief that certain areas of the cerebral cortex were particularly concerned with intelligence. Physiologically, he looked upon the frontal lobes as having motor functions, the precentral portion being excitatory, the antero-frontal, inhibitory. Psychologically they were regarded as centers of attention, a process through which the "intellectual and reflective powers" were manifested.

The trend toward localization of higher psychic functions had already found supporters among clinicians of the times as well as in the experimental laboratory. Among the experimental physiologists, Hitzig and Ferrier were able advocates of the doctrine of localization. In discussing Munk's views of the cortex, (Hitzig in 1884 (23)) reaffirmed his earlier extreme position by writing:

"I find myself in opposition to Munk as regards the nature of the higher intellectual functions and their relation with the anatomical substratum. Munk holds that there are not special organs for these functions and that there is no necessity for them. I believe with him that intelligence, or more correctly the treasury of ideas, is to be sought for in all parts of the brain; but I hold that abstract thought must of necessity require particular organs and these I seek provisionally in the frontal brain" (Quoted from Bianchi (1, p. 71)).

## I. THE FUNCTIONS OF THE FRONTAL ASSOCIATION AREAS IN MONKEYS

C. F. JACOBSEN

### HISTORICAL SETTING OF EXPERIMENTS

Theories of cerebral function since early formulations by Gall and Spurzheim have represented two distinct points of view and it has been with varying fortunes that advocates of localization and of omnivalence have endeavored to establish the correctness of their respective doctrines. In these discussions the rôle of the association areas—the frontal and prefrontal in particular—has been a point of recurring controversy. That the frontal lobes have continued to be recalcitrant to experimental study in animals to a greater degree than sensory and motor regions of the cortex has been due, in no small measure, to the indefinite nature of the defects associated with injury of this region. Moreover, it is only as special behavioral techniques are employed that occasion arises to modify greatly Ferrier's classic characterization of frontal lobe deficit in monkeys. In 1876 he wrote:

"Removal or destruction by cautery of the antero-frontal lobes is not followed by any definite physiological results. The animals retain their appetites and instincts, and are capable of exhibiting emotional feeling. The sensory faculties, sight, hearing, touch, taste and smell remain unimpaired. The powers of voluntary motion are retained in their integrity, and there is little to indicate the presence of such extensive lesions, or removal of so large a part of the brain. I have removed the frontal lobes . . . almost completely in three monkeys, with the same negative results, and what is more remarkable, I found that the removal of these lobes in an animal which had recovered from ablation of the occipital lobes caused no symptoms indicative of affection or impairment of the special sensory or motor faculties.

"And yet notwithstanding this apparent absence of physiological symptoms, I could perceive a very decided alteration in the animal's

altered intellect, all the more severely, the more extensive the injury since a larger group of images having their foundations in the destroyed area would be lost. The superficial similarity between Munk's view and certain of Lashley's later formulations is readily appreciated.

Luciani (44) admitted the need of association areas for higher psychic processes, but denied such functions to the frontal lobes, and in harmony with Munk, regarded them as centers for the musculature and sensibility of the neck and back. Luciani's position was supported by the researches of Sciamanna, Polimanti (see (1)) and Horsley and Shaefer (24). These investigators reported but slight and transitory disturbances in dogs and monkeys after injury to the frontal lobes, but their denial of higher functions to this region was challenged because the lesions involved only small portions of the frontal and prefrontal areas.

In more recent times, the doctrine of localization of higher psychic functions has been ably and persistently advanced by Bianchi (1) who has elaborated the earlier views of Hitzig into a theory of hierarchies of correlation centers of which the frontal lobes form the highest level. While he recognized the important contributions of the temporal and parietal association areas to the formation of intellect, greatest dignity and importance were assigned to the syntheses mediated by the frontal lobes. Bianchi concluded from his experiments and clinical observations:

"Removal of the frontal lobes does not so much interfere with the perceptions taken singly, as it does disaggregate the personality, and incapacitate for serializing and synthesizing groups of representations. The actual impressions, which serve to revive these groups, thus succeed one another disconnectedly under the influence of fortuitous external stimuli, and disappear without giving rise to associational processes in varied and recurrent succession. With the organ for the physiological fusion which forms the basis of association disappear also the physical conditions underlying reminiscence, judgment, and discrimination, as is well shown in mutilated animals."

Presumably this diminution in synthesizing capacity is a quantitative loss, and according to this view, the association centers

The controversy, which remains alive at the present day, was vigorously launched and efforts to localize higher functions in the frontal lobes did not go unchallenged. Goltz emphatically denied that injury to the frontal parts of the brain in dogs caused more severe dementia than injury to the posterior parts, and emphasized the relation between the degree of impairment and the extent of cortical destruction. Loeb (42) later concurred in this view and argued that "localization of psychic functions in the cortex is opposed to the elementary facts of associative memory or consciousness." In refuting claims that intellect is a function of specialized regions of the brain Loeb states:

"The assumption of 'centres of association' is just as erroneous as the assumption of a centre of coördination in the heart. Association is, like coördination, a dynamical property determined by the conductivity of the protoplasm. Associative processes occur everywhere in the hemispheres (and possibly in other parts of the brain), just as coördination occurs wherever the connection between two protoplasmic pieces is sufficient" (42, p. 275).

In reviewing neurological theories of intelligence, Lashley (34) has shown the weakness of the dynamic theories of Flourens, Goltz and Loeb in that they do not explain the characteristics of deterioration in any form of dementia, and offer no conceptions of how a unified mass of nervous tissue may participate in qualitatively diverse activities with an efficiency solely proportional to its quantity.

Munk's theory, based upon sensory localization in the cortex, offers a more satisfactory formulation of the doctrine of omnivalence than the dynamic views of Flourens, Goltz and Loeb. Munk (51) divided the cerebrum into a number of sensory spheres in which the images associated with a given sensory modality were stored and elaborated. According to this view, complex integrations and intersensory correlations were effected by interconnections between sensory spheres, and the existence of specialized areas of association for the higher intellectual functions was denied. Intelligence was regarded as the product of the several sensory spheres, and any considerable lesion of the cortex

→ 6. "Only newly formed habits seemed lost after such lesions. Long-standing habits seemed to be retained."

→ "From clinical and experimental results of others as well as those which have been recorded in the present paper I conclude that the frontal lobes are concerned in normal and daily associational processes and that through them we are enabled to form habits and, in general, to learn" (16, pp. 63-64).

At first glance these experiments seem to support Bianchi's contentions since there was amnesia for recently acquired sensory-motor associations. However, the fact that Franz's animals were able to relearn the habits in normal time opposes Bianchi's claim that animals which suffer removal of the frontal lobes show marked diminution in learning ability. But more strongly in contradiction are the records of animals which showed no amnesia for recently acquired habits. These negative instances Franz explained on the hypothesis that through over-training the habits were mediated by lower centers, an assumption which has been shown (25) to be poorly substantiated by Franz's own protocols. Bianchi dismissed Franz's negative results on the grounds that the lesions involved only part of the frontal association areas. The autopsy reports are not adequate to determine the validity of this criticism.

The writer (25) has recently determined the effect of frontal lobe lesions on acquisition and retention of sensory-motor habits, using as test situations puzzle boxes of varying degrees of complexity and visual discrimination problems. He failed to confirm Franz's claim that recently acquired habits were lost after frontal injury since there was no amnesia for simple problem box and visual discrimination habits. The acquisition of new sensory-motor habits after operation took place at normal rate and in no instance when lesions were restricted to the frontal association areas was there general deterioration of behavior.

It is evident that studies of the frontal association area in monkeys have produced a diversity of opinion concerning its functions. The effects of injuring this region embrace a wide range of symptoms: by some investigators, removal of the frontal lobes has been described as causing "no intellectual impairment,"

of the frontal lobe add only a final stage of integration to connections established in the more posterior parts of the cerebrum. They are coordinating centers rather than regions for special elaboration. Certainly the impression Bianchi strives to produce by his protocols is one of general dementia rather than the loss of a specific function. In this view Brickner (4)<sup>1</sup> concurs after an excellent and thorough analysis of the behavioral defects in man following bilateral frontal lobectomy, and indicates that "all of the interpretable changes may be explained by a diminution in the associative function of synthesizing simple mental engrams into more complex ones. Hence, the changes are fundamentally quantitative in character, and not qualitative."

Bianchi's experimental observations on the functions of the frontal lobes in monkeys are vulnerable at two points: (a) his experiments are impressionistic—objective measures of the degree and nature of behavioral deficit are lacking; and (b) he has not demonstrated that lesions of equal extent in other parts of the cortex do not cause dementia of equal severity.

(1957) The work of Franz (16), building on the earlier studies of Hitzig and Bianchi, is especially noteworthy because he first applied the objective techniques of comparative psychology in measuring behavioral deterioration after cortical injuries. His results on the effects of frontal lobe injury are briefly summarized:

1. "In monkeys and cats the frontal lobes are normally employed in the formation of simple associations.
2. "When the frontal lobes are destroyed recently formed habits are lost.
3. "The loss of associations is not brought about by lesions of other portions of the brain.
4. "The loss is not due to shock, for lesions of other parts of the brain are not followed by loss of the habits nor does the anesthetic and loss of blood, etc., produce loss of the association.
5. "Habits once lost after removal of the frontals may be relearned. The relearning takes about as long a time as if the animal were relearning a new association.

<sup>1</sup> No attempt has been made to include clinical materials in this summary; for a discussion of recent clinical observations on the frontal lobe the reader is referred to Brickner's (4) study.

A.G.R.

"monkeys  
problems"

training so that the usual visual functions of the striate area were not activated at the time of acquisition of the habit, indicate that deterioration is of the same magnitude as for those animals in which it had served its normal visual functions (55, 56). It thus appears that in the rat a given cortical area may participate in two distinct patterns of organization: one in which the differentiated structure is predominant, and another in which the functionally undifferentiated mass of tissue is of greater significance.

The application of the principles of equipotentiality and of mass action, as illustrated in cortical activity in maze learning by rats, to human neurology has not met general acceptance. Evidence for diffused function in man is most readily gathered from cases with deterioration at complex levels of integration. In these instances the disturbances are often vague and poorly defined, and similar symptoms seem to arise from lesions in quite diverse parts of the cortex. On lower functional levels in primates, e.g., motor and sensory projection systems, it is clear that not all parts are functionally equivalent; but at the so-called higher levels, specialization of function and restriction to limited areas has not been established.

This paper presents a series of experimental observations on the rôle of the frontal association areas in the organization of behavior in lower primates. Two interrelated problems are involved: the one is neurological, the other psychological, and solution of the former may supply, in part, an answer to the latter. From a neurological point of view, we may ask: Do the frontal association areas mediate a type of behavioral adaptation which the organism is incapable of exhibiting in the absence of this region? Is this contribution something which is peculiar to the frontal lobes, or do the behavioral deficits also appear after equally extensive injuries in other parts of the cortex? In a more general form, we may ask: Do the principles of equipotentiality and of mass action which Lashley has demonstrated at the more complex levels of integration in the rat, also characterize cortical organization in primates? The problem here raised for study by psychological means is similar to that attacked by Poliak (52) from

but by others, as causing profound deterioration of all intelligent behavior. From these experiments certain conditions requisite to adequate experimentation can be specified, e.g., selection of appropriate behavioral tests, restriction of lesions to the frontal areas, and introduction of control lesions in other cortical regions.

#### STATEMENT OF PROBLEM

In the last decade the work of Lashley and his students has again challenged the doctrine of cortical localization, especially as applied to higher levels of integration. In brief, these investigations have shown that in rodents a given cortical area may subservise two different functions and participate in two different plans of cerebral organization. Thus, the area striata is the region of primary projection for fibers of the visual system arising in the lateral geniculate body. Recent anatomical studies (37, 38) have demonstrated that this area exhibits a mosaic localization which in detail of representation and rigidity of organization approaches that of the corresponding region of the primate brain (6, 7). Lesions in this area cause more or less severe impairment of visually determined behavior although injury in the anterior two-thirds of the cortex does not produce such deterioration. These experiments have indicated marked anatomical and functional specificity of the striate area for visually controlled reactions that are organized at cortical levels.

However, the area striata also participates in the associational activities of the cortex in a manner different from and seemingly independent of its functions as a visual projection field. Thus retardation in learning of complex mazes (34, 41) and other problems involving temporal organization of behavior (43, 46, 47) is proportional to the mass of cortical tissue destroyed but is relatively unrelated to the locus of the lesion. It appears that for this type of integration, which is not dependent upon a particular sensory region but involves temporal patterning of behavior, the various cortical areas are, within wide limits, functionally equivalent. Injury to the occipital third of the cortex retards maze learning, but no more so than do lesions in other parts of the neo-cortex. Control observations on animals blinded before

to varying the kind or amount of food, or the degree of satiation in the study of animal motivation.

In the present experiments three groups of behavioral tests have been employed: (a) problem boxes requiring the establishment of stable visuo-kinesthetic-motor habits; (b) visual discrimination problems; and (c) delayed response. In the first two groups of tests, the subject is confronted on successive trials by a problem situation which presents the necessary differential cues at the time of response. Thus in comparison and selection between two visual patterns, differential cues impinge upon the animal's sensorium from the test situation itself. Once the subject has learned that food can be obtained from the larger of two paired boxes, the differential cues which determine for a given trial whether the right or left box shall be opened, are inherent in the test situation. In a similar way, each problem box offers to the sophisticated subject differential cues which release motor activities appropriate to the particular task.

In testing for delayed response, the differential cues which determine whether the right or left box shall be opened are carefully eliminated from the test situation and must in some manner be supplied by the subject. In the direct method of testing for delayed response, the subject observes the experimenter conceal food under one of two similar test objects. Before there has been opportunity to make a completed response, an opaque door is interposed between subject and test objects, and only after an interval of a few seconds to several minutes is the subject permitted to open one of the two paired test objects, and if its choice has been correct, obtain the food which it earlier saw concealed. In a properly controlled experiment visual, olfactory, or other cues are not inherent in the test situation, and by contrast with discrimination and problem box tasks, the differential cues that determine which particular test object will be selected, must be supplied by the subject either through some sustained activity during the period of delay or by recall from past experience, i.e., observation of the experimenter concealing food at the beginning of the trial.

That the tests employed in the present experiments make dif-

fer from the neuro-anatomical point of view. In his extensive study of the afferent fiber systems of the primate brain, he writes:

"My previous and present investigations justify admission of the existence of differences in functional significance of the specific afferent paths of the cerebral cortex, and even of the individual small neuron units composing each of the somatic sensory, auditory, and the visual systems together with their respective cortical terminal areas. Moreover, it appears logical as a next step to admit the existence of some kind of localization of "higher" activities in the chain or sequence of events interposed between initial afferent processes and final efferent acts. . . . Nor does it seem possible to avoid such a conclusion, however risky this might appear and difficult to solve, if we consider the advanced structural differentiation of the human cortex as compared with that in lower mammals. . . . Nevertheless, as previously stated, the difficulty here is not only in discovering special structures, the substrata of particular primitive functions, but also in determining and in defining of those primitive or elementary processes to be localized. Be this as it may, advance in the disentanglement of these intricate problems may be expected from further investigation of the organ of the mind itself and by improved methods of study rather than from elaborate speculation" (52, pp. 217-18).

The psychological aspect of the investigation has been anticipated by Poliak's pointing, in the above quotation, to the difficulty "in determining and defining of those primitive or elementary processes to be localized." However, detailed consideration of this problem can profitably be reserved until the neurological findings have been presented, since it is our purpose to base psychological analysis upon neuro-physiological experimentation. It is well to note, however, that the problem raised and the answer sought are psychological—not neurological. This is a point about which confusion exists in the minds of some psychologists who tend to dismiss the neuro-physiological approach as perhaps interesting and valuable, but essentially not psychological. To place this interpretation on the experiments is erroneous. Experimental injury to the nervous system is here utilized as a tool of psychological analysis, as an added variable comparable in character

and the corresponding part of the superior gyrus on the medial aspect. Its anterior limit is found in the monkey in the superior limb of arcuate and its arbitrary extension to the midline. The posterior boundary is variable but corresponds roughly with the superior precentral sulcus. There is also a small premotor area oral to the motor area for the face. Microscopically the premotor area is similar to area 4 except for the absence of the large Betz cells. The third and fifth layers, which tend to fuse in places, contain large pyramidal cells (although smaller than the Betz cells) throughout area 6.

*Frontal region.* Microscopically in man and in monkey the frontal region forms a counterpart of the precentral since it is characterized by the presence of an internal granular layer. In monkeys this region occupies the anterior half of the frontal lobe; in man it comprises more than four-fifths of the lobe. Five areas or fields have been recognized:

(a) Area 8 (area frontalis intermedia, area FC, the eye-fields). Area 8, both on the grounds of its transitional architectonic arrangement and of its functional characteristics, might well be regarded as a part of the motor-premotor complex. It extends as a narrow strip along the forward rim of the arcuate sulcus, and the frontal region accordingly presents a wholly different arrangement than in man in whom area 8 occupies the space rostral to the premotor region on the convexity of the hemisphere.

(b) Area 9 (area frontalis granularis, frontal area of Campbell, area FD). Area 9 of the simian brain corresponds in arrangement and structure with areas 9 and 10 of the human cortical map of Brodmann. In the monkey area 9 constitutes the greater part of the frontal region on the lateral and medial aspects.

(c) Areas 10 and 11 (areas orbitalis externa and interna, FG and FH). These areas make up the orbital surface of the frontal lobe.

(d) Area 12 (area frontopolaris, prefrontal area of Campbell, area FE). Area 12 occupies the tip of the frontal lobe and corresponds to area 11 or the prefrontal area of the human cortex.

The homologies of these fields in man and lower primate is not clearly determined, although Brodmann has indicated that the structural characteristics of fields 44, 45 and 46, the speech areas of the human brain, are not found in the monkey. It is thus the

erent demands upon the organism is fairly clear, although definition and identification of the psychological functions involved is less evident. Beyond suggesting at this time that the distinction thus made in operational terms parallels the usually accepted distinction between the psychological functions of recognition and of recall, consideration of this topic can better be reserved until discussion of the experimental findings.

#### SOME ANATOMICAL AND PHYSIOLOGICAL CONSIDERATIONS

The frontal lobe of primates consists of that part of the neopallium which lies anterior to the central sulcus. This major part of the cortex has been divided into several regions and areas which have distinctive cytoarchitectonic characteristics (see Brodmann (5); Campbell (12); von Economo (13); C. and O. Vogt (57)). Of these several studies, that of Brodmann is of greatest significance for present consideration since it offers the most complete homologous analysis of the frontal lobe in man and monkey. In Brodmann's classification two regions, precentral and frontal, each consisting of several smaller areas or fields, are recognized.

*Precentral region.* The posterior boundary of the precentral region is found in the central sulcus, whence the region extends rostrally to occupy in the monkey about one-half of the frontal lobe in contrast to scarcely one-tenth in man. The precentral region is composed of two closely related cytoarchitectural fields, namely: the motor and premotor areas (areas 4 and 6 of Brodmann respectively).

(a) Area 4 (motor area, area gigantopyramidalis, area FA of von Economo). The motor area in the monkey occupies the anterior wall of the central sulcus and several millimeters of the dorsal convexity of the precentral gyrus. Microscopically this area is composed of essentially five layers since the internal granular layer is absent or greatly reduced. The outstanding characteristic is the presence of the gigantic pyramidal cells of Betz.

(b) Area 6 (premotor area, area frontalis agranularis, area FB, intermediate precentral region of Campbell). The premotor area occupies the region rostral to the motor area and superior to the arcuate sulcus

sented in a cage with two adjoining compartments (fig. 1). Passage between the delay (*A*) and reaction (*B*) chambers was controlled by two porteullis doors, one a grille (*G*) through which the subject could see the preparation of the problem (as illustrated,

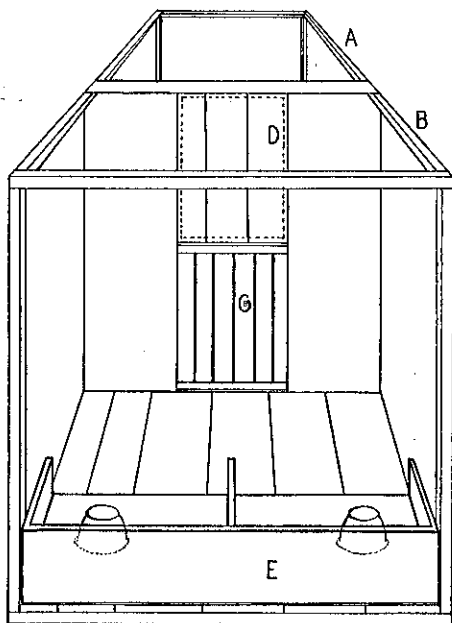


FIG. 1. FLOOR PLAN OF EXPERIMENTAL CAGE

*A* and *B* denote the delay and reaction compartments; *G* is a porteullis grille, and *D* an opaque door. The tray and cups, *E*, used for the delayed response are shown in position. The problem boxes and visual discrimination apparatus are substituted for the delayed response equipment.

the delayed response), and the second, a solid door (*D*) for completely interrupting vision between compartments. The sides and top were made of 3 cm. wire mesh, the floor and partition (*P*), which enclosed the controls for the doors, of unpainted pine. A one-way vision screen, placed 3 feet in front of the reaction com-

third frontal gyrus and the middle portion of the second frontal gyrus which appear to be lacking.

In the following sections of this monograph we shall use the terms frontal areas and frontal association areas interchangeably to refer to that part of the frontal lobe of the monkey embraced in areas 9 and 12 of Brodmann (frontal and prefrontal areas of Campbell, areas FD and FE of von Economo). The frontal areas will be treated as a unitary region without attempting at present to make functional differentiations between the several fields.

In addition to architectonic evidences, abundant functional data give support to the division of the frontal lobe into the precentral and frontal regions (1, 2, 9-11, 17-22, 26, 32, 53, 54). Consideration of these and earlier studies of the frontal lobes makes it evident that the following neurological requirements must be met: (a) Lesions must be restricted to the frontal association areas, since any extensive encroachment upon the precentral region markedly modifies the characteristics of behavioral deficit. In the present experiment the arcuate sulcus and its arbitrary projection to the mid-line was accepted as the posterior boundary of the frontal areas. (b) The effects of lesions of equal or greater magnitude in other parts of the cortex must be observed. In the present paper, experiments dealing with injury to the precentral region, the postcentral areas, posterior parietal region, and the temporal lobe, will be presented or cited by reference.

#### SUBJECTS AND EXPERIMENTAL METHODS

##### *Subjects*

Several species of monkeys were used as experimental subjects (*Macaca mulatta*, *Cercopithecus torquatus* and *Papio papio*). Details of age, sex, adaptation to experimental procedures, etc., are indicated in the protocols for individual subjects.

##### *Tests and training procedures*

*Training cage.* The several problem situations—problem boxes, delayed response and visual discrimination—were pre-



so that S faced the crank in its former position. These readjustments were made with little difficulty. The pull and the hook and handle could be opened either first or second, whereas the crank, which had to be raised above the lowest point of the arc and consequently could fall back, of necessity had to come last in the series.

*Delayed response.* The delayed response tests employed the direct situation. With S in the delay compartment, the solid door was raised and there was thus exposed through the grille a black tray containing two white cups 60 cm. apart (fig. 1). E then attracted S's attention to one of the cups by placing food beneath it. After an interval, the grille door was raised and S entered the forward compartment to make its selection between the cups, and if correct in its choice, secure the food which it had earlier seen concealed. When an accuracy greater than 80 per cent had been achieved and S seemed well adapted to the training procedure, the solid door was lowered during each trial, as soon as the cup had been baited, and remained in the lowered position during the delay period. The grille and solid doors were successively raised at the end of the period and S advanced to the reaction compartment as indicated above. Training was continued until S responded correctly on more than 80 per cent of the trials after delays of five to ten seconds measured from the time the food was placed under the cup until the doors were raised.

Since it was our purpose to compare performance before and after cortical extirpation, conditions were established under which several series of comparable tests could be made to determine levels of performance for various delay intervals. At the completion of the initial training indicated above, S was given thirty trials per day with the length of delay determined according to this plan:

RS	IS	RS
LM	LL	RM
LL	LM	LL
RM	RS	RM
RL	LL	RL
IS	RS	RM
LM	RL	IS
RL	RM	LM
LM	LL	LS
RS	IS	RL

partment, enabled E<sup>2</sup> to observe S's behavior and by means of ropes and pulleys, to control the doors between chambers without disturbance of work or introduction of secondary visual cues.

*Problem boxes.* Five problem boxes varying in difficulty were employed. Since these boxes and the training procedure have been described elsewhere (25, pp. 278-282), only brief characterization will be given at this point. S was taught to seek food from open boxes until it was thoroughly accustomed to the situation. The latch of the box was then closed and S's efforts at solution of the problem noted, especially handedness, use of teeth, perseveration of useless movements and peculiarities in manipulation.

The following boxes, linear dimensions about 18 x 12 x 12 cm. were used:

*Rope box.* To open this box S must pull a rope projecting from the right side of the box.

*Pull box.* S must reach through a hole and grasp and pull a rod which passed transversely across the opening. Pulling this rod toward the operator released the lid.

*Crank box.* S must grasp and turn a crank projecting from the front of the box. The crank, which described a circle 10 cm. in diameter, was set at "11 o'clock," and had to be turned through 270° clockwise to release the lid.

*Hook and handle box.* S must raise a handle at the front of the box. The handle was set at "3 o'clock" and had to be turned through 60° counter-clockwise to permit unfastening of a hook. After unfastening the hook, S had to raise and hold the lid while removing the food. The handle could be locked at the "1 o'clock" position after it had once been raised beyond that point. Because of the difficulty of this problem for monkeys, ten trials with only the hook were given before introduction of the handle.

*Serial combination box.* The latches of the preceding three problems were combined on one box. The pull and the hook and handle were left in their former positions, but to facilitate construction, the crank was moved to the right side of the combination box. This change necessitated slight readjustment of the methods of opening, such as a shift from the left to the right hand or a change in the position of the body

\* In the present and following sections, E and S will designate experimenter and subject.

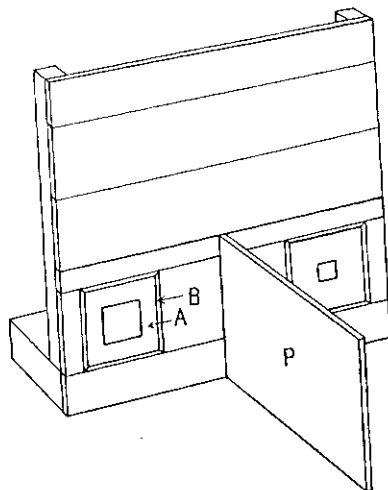


FIG. 2A

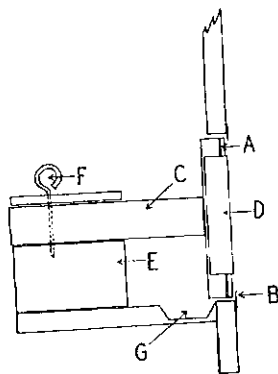


FIG. 2B

FIGS. 2A AND B. DETAILS OF VISUAL DISCRIMINATION APPARATUS. The following symbols are used: A, stimulus card; B, limiting flange; C and D, carrier and holder for stimulus card; E, track for carrier; F, locking device; and G, food tray. The entire apparatus, as shown in b, is fitted into the front opening of the reaction compartment. The partition, P, separating the two stimuli, extends 45 cm. into the cage.

The first letter of each pair refers to the right or left cup; the second, to the length of delay. On a given day three delay intervals were employed in order to encourage sustained effort by counteracting failures on longer delays with more frequent successes after shorter intervals. Thus on the first day, intervals of (S) 15, (M) 30 and (L) 45 seconds might be used; on the next day, (S) 30, (M) 45, and (L) 60; and so on, until by progressive steps values were reached that gave results approximating 50 per cent correct choices. At the end of this series, tests with short intervals were given to assure that failure had not been due to breaking down of S's set for the problem.

The daily results at various lengths of delay were summed at completion of the tests, and the percentage of correct choices determined for total trials. The percentages for the middle group of delay values are consequently based on a greater number of trials since the intermediate values were used as S, M, and L items in contrast to the extremes which appear only as S or L.

*Visual discrimination.* For testing visual discrimination the principle of Lashley's jumping technique (36) was adopted and an apparatus suitable for monkeys arranged as indicated in figures 2a and 2b. In this procedure S was required to push directly against a stimulus card (A) in order to get food concealed behind the card. During initial training, S was allowed to take food from the food tray with the carrier (C) and stimulus card (A) in the open position, i.e., pushed back to give free access to (G); on succeeding trials the test card was gradually moved forward until S was accustomed to operating the carrier. The limiting flanges (B) cut down the exposed card to a 20 x 20 cm. square. The stimulus cards were made of Upson Process Board, 22 x 22 cm., painted with black enamel. Squares of white, 2, 4, 8, 12, and 16 cm., linear dimensions, were painted on black backgrounds.

Training on discrimination began with a white 8 cm. square (positive) versus a plain black card. With the monkey in the delay compartment and the solid door lowered, food was placed in the tray, and the test cards pushed into position against the flanges. The door was then raised and the animal allowed to make its choice between the two test objects. Touching and

*Verification of lesions*

On completion of postoperative tests, the animals were sacrificed at autopsy. The graphic representations of the lesions (figures 3, 4 and 5) are based on three sources of information: gross and histological examination of the brain at autopsy, the extirpated tissue, usually removed in a single block with the major topographic markings preserved, and the cellophane tracing made at operation. Although the use of the cellophane tracing can not supplant the usual histological examination either by sample blocks or serial sections, it has proved to be a valuable adjunct in reconstructing the lesion. Extensive ablations are not infrequently followed by distortion of landmarks through shifting of cerebral substance in the brain case or filling in of the extirpated area. Thus, in experiment 4 (fig. 5), the linear measurements of the lesion between *a* and *b* were 30 to 40 per cent less at autopsy than at operation, and a description based solely on the fixed brain might cause considerable underestimation.

The following abbreviations for sulci and fissures have been used on all figures: *A*, arcuate; *C*, central; *F*, frontal; *PO*, parieto-occipital; and *S*, Sylvius. Extirpated or degenerated regions are indicated by stippling. All drawings are reproduced at approximately natural size.

## RESULTS

Protocols of four experiments are presented. The data will be considered under the following topics: (1) preoperative training, (2) operation and recovery, (3) interoperative tests, if the lesions were produced in two stages, (4) second operation and recovery, (5) postoperative tests, and (6) verification of lesions.

*Experiment 1. Simultaneous bilateral extirpation of frontal areas.  
(Frontal II)*

The subject of this experiment was an immature female monkey (*Macaca mulatta*) which had been under observation for six weeks before training on special problems was undertaken. Its weight was 3000 grams.

*Preoperative training.* Preoperative training included mastery of

pushing the negative card was scored as an error. Thirty trials per day were given except when specifically noted in the protocols. The order and pairing of stimulus cards are considered for individual subjects.

*Surgical procedures*

Anesthesia was induced by intraperitoneal injection of sodium amytal, after which the operative field was prepared by shaving and cleaning the scalp with bichloride and alcohol sponges. Aseptic precautions were observed throughout. A large bone-flap, over one or both hemispheres, was turned back and after reflection of the dura, a cellophane tracing of the chief cortical markings, i.e., fissures, sulci, and blood vessels, was made. The limits of the proposed lesion were outlined at this time in reference to these landmarks.

Extirpation of cortical tissue was accomplished by first coagulating the large vessels passing into the sinus with the Davis-Bovie electro-surgical unit, and then incising the boundaries of the proposed lesion with the cutting current. Bleeding from arteries was controlled with fine silver clips. The last stage of extirpation was effected by carefully dissecting away the cortical tissue with blunt spatulas. If possible, the tissue was removed in a single block and preserved for histological examination. When compatible with experimental and surgical requirements, sulci and other fixed landmarks were used to circumscribe the lesion.

Closure of the wound was effected by drawing the dura over the cortex and suturing lightly with interrupted silk stitches. The approximated bone flap was then firmly secured by suturing the temporal muscles and aponeurosis with interrupted stitches. In the last step the approximated edges of the skin were fastened with interrupted sutures and finally closed with continuous subcutaneous suturing. After covering the wound with an alcohol sponge, the animal was returned to its cage where body temperature was maintained by placing warm bottles with the animal until it had recovered from anesthesia, usually a matter of four or five hours. Further details concerning these surgical procedures are given elsewhere by Fulton and Keller (18).

**Pull box.** S simultaneously grasped the pull rod in the left hand and rested the right on the lid, which was raised as soon as the catch had been released. Food was taken with the left hand. Time was about one second. Postoperative retention of the pattern of response was excellent and there was no increase in time required.

**Crank box.** S consistently used the left hand to turn the crank, sitting in front of and slightly to the right of the box. The crank was usually turned with one uninterrupted movement through 270° and fumbling and reversal of direction rarely occurred in later trials. Average time was slightly under two seconds. Retention of the responses to this box was not impaired.

**Hook-handle box.** The left hand was used for raising the handle, releasing the hook and raising the lid. Time required was about two seconds. In the postoperative tests S did not respond readily to the handle on the first few trials, spending most of its energies in attempting to release the hook, but the tendency to neglect the handle disappeared within five trials. Retention of this habit was disturbed but slightly.

**Combination box.** Preoperative performance on this box was irregular in time consumed, ranging from quicker times of five to eight seconds to as long as twenty or thirty seconds on a few trials. S shifted frequently from one latch to another without tendency to persevere on a given latch to the neglect of others. In the postoperative tests there was an increase in time required and a pronounced tendency to persevere in manipulation of a latch which had been opened and to neglect entirely other latches. It should be noted, however, that when presented singly, S was able to manipulate skillfully each of the latches which offered trouble in combination.

**Delayed response.** In the initial preoperative training on delayed response the two cups remained in S's field of vision during the delay period. Twenty-nine correct choices after delays of five seconds were made in thirty trials. Further training with vision interrupted during delays of five to fifteen seconds followed. When S had reached the desired stage of proficiency, two series of tests, separated by an interval of three months, were given. Inspection of the results, presented in table 1, indicates that S made progressively fewer correct responses as the length of delay increased, and that the percentage of correct responses after delays of twenty-five seconds in the first series, and thirty seconds in the second, did not differ reliably from chance.

In addition to lower scores after longer delays, other evidences indicated that S had approached the limit of its ability under conditions of

problem boxes and testing for delayed response. Significant features of these adaptations will be considered in relation to behavioral changes after operation.

**Operation and recovery.** The animal was anesthetized with an intraperitoneal injection of sodium amytal, 0.5 cc. of 10 per cent solution per kilogram body weight. Large bilateral bone-flaps were turned down to expose the dorsal surfaces of both hemispheres. After reflection of the dura of the left hemisphere, the chief cortical markings were traced on cellophane, and the tissue lying anterior to the arcuate sulcus and its arbitrary extension to the midline removed in one piece. A similar procedure was followed in making a symmetrical lesion in the right hemisphere. Closure was effected in the usual manner.

S had recovered from anesthesia the following morning; it was alert, and vocalized and gestured as usual. There was no motor deficit and no evidence of asymmetry. On the second day edema over the temporal muscles and scalp developed and persisted for five days although S remained alert and active. Healing of the wound was satisfactory and physical condition excellent.

**Posture, motor power and forced grasping.** Bilateral destruction of the frontal areas produced no permanent alteration of posture and no deficit in motor power in any extremity. At no time was there evidence of forced grasping and groping.

**Spontaneous activity.** S exhibited great increase in spontaneous motor activity with rather constant restlessness, interrupted by periods of little or no activity under reduced external stimulation as described elsewhere (25). This heightened activity persisted until termination of the experiment nine months later. With augmentation of motor activity, there was an increase in quantity of food ingested, although basal metabolic rate was no higher than that of normal monkeys (8).

**Postoperative tests.** Retention tests of problem box habits and of delayed response were undertaken ten days after bilateral removal of the frontal areas, and were repeated from time to time during the following nine months.

**Problem boxes. Rope box.** The typical solution of this problem consisted of picking up the rope with either the right or left hand, placing it in the mouth and pulling the rope by moving the body away from the box. The lid was then raised with the right or left hand. Time required rarely exceeded two seconds. On the first postoperative tests, S showed the same characteristic pattern of behavior, and there was no indication of impairment either in increased time or in fumbling with the latch.

on the tenth day after operation, at which time the animal was alert, active and eager for food, and had already successfully manipulated the simpler problem boxes. S showed good adaptation to the general features of the delayed response situation, i.e., sought food under the cups, and shifted from reaction to delay compartments upon command. As in the preoperative training, the initial trials were made with only the grille door, thus permitting the animal to maintain its visual orientation toward the test objects until the time of response. Under these conditions, twenty-four correct choices were made in forty trials—60 per cent accuracy in contrast to 97 per cent correct responses in the initial period of the preoperative training. In the first twenty trials errors were made to both the right and left; in the last twenty, a marked right preference predominated. Although S apparently watched closely while the cups were loaded, it vacillated between the test objects when making its choice in contrast to the previously direct approach regardless of the correctness of the choice. The grille door was then eliminated and S was restrained in the delay compartment by a light rope attached to its collar. As the cups were loaded S was released and it walked without interruption or disturbance toward the cups. Under these conditions S was given twenty-eight opportunities. It responded correctly on 86 per cent of the trials. The average time between concealment of the food and choice was slightly more than three seconds. Following the sixth and sixteenth trials, ten trials under the usual conditions—grille door in use—resulted in only eight correct choices in twenty trials although the delay did not exceed by more than two seconds the delays introduced by the animal in making its choice in the absence of the grille door. During these trials motivation was good, and S appeared to be making an effort to select the correct cup.

Training was discontinued until the seventh week following operation when additional trials, ten per day with greater amounts of food, yielded no better results: a chance score of 50 per cent in fifty trials with only the grille door in use and 45 per cent in twenty trials with both doors lowered during delay.

Again at fourteen weeks and at nine months, efforts were made to test and train the animal but over 120 trials yielded results essentially the same as those recorded above. At the end of nine months, S was subjected to a second operation involving destruction of the premotor areas. Its subsequent history will be reported in relation to studies of this area.

*Verification of lesions.* Examination of the brain *in situ* at later

these tests. On longer delays it frequently failed to make a choice or did so only after being coaxed, although it continued to respond readily after interspersed shorter delays. Expressions of rage became frequent with longer delays. However, vacillation between cups rarely occurred on either short or long delays; the animal went directly to one of the cups regardless of the correctness of its choice. It is significant to note, in view of the postoperative restlessness, that bodily orientation or

TABLE I  
Summary of preoperative tests on delayed response showing number of trials, per cent of correct choices, and reliability of the difference between obtained values and the assumed chance value of 50 per cent  
Delay periods between five and forty seconds. (Frontal II)

	PERIOD OF DELAY IN SECONDS					
	5	10	15	20	25	30
Preliminary training						
Number of trials.....	20	50				
Per cent correct.....	90	90				
First series						
Number of trials.....	50	80	70	60	30	
Per cent correct.....	96	90	81	70	63	
Diff./ $\sigma_{diff}$ .....	5.9	6.1	3.9	2.3		
Second series						
Number of trials.....	60	20	40	60	60	30
Per cent correct.....	98	100	85	78	70	63
Diff./ $\sigma_{diff}$ .....	7.0		3.6	3.3	2.3	

\* The period of delay varied slightly from one trial to another, and delays indicated as ten seconds were not less than ten nor more than fifteen seconds in length. A similar range of five seconds applies to the other intervals.

constant position in the cage was not essential to S's performance, and that during the delay period it frequently walked and climbed about the cage. It was not unusual for S to observe baiting of a cup by looking over its shoulder while facing the back of the cage and yet make its choice correctly after turning around several times during the delay. Activity *per se* did not disturb the animal.

Bilateral extirpation of the frontal areas profoundly modified adjustments to the delayed response test. Examination was first undertaken

*Operation and recovery.* Under sodium amytal anesthesia, supplemented by ether, a large left-sided bone-flap was turned down, exposing a highly convoluted cortex. The dura was reflected, and the chief markings traced on cellophane. The extirpation was carried out with the Davis-Bovie electro-surgical unit by first coagulating the veins leading to the sinus and by placing a silver clip on the branch of the anterior cerebral artery supplying the block of tissue to be removed. The arcuate sulcus was then incised, and the incision carried directly to

TABLE 2

*Summary of preoperative and interoperative tests on delayed response showing number of trials, per cent of correct choices, and reliability of the difference between obtained values and the assumed chance value of 50 per cent*

*Delay periods between ten and one hundred twenty seconds. (Frontal V)*

	PERIOD OF DELAY IN SECONDS						
	10	20	30	45	60	90	120
<b>Preoperative tests</b>							
Number of trials.....	40	30	50	60	60	30	30
Per cent correct.....	100	97	90	88	75	67	53
Diff./ $\sigma_{diff}$ .....		5.0	4.8	5.1	2.9		
<b>Interoperative tests: First series</b>							
Number of trials.....	60	40	60	60	60	30	30
Per cent correct.....	85	98	87	82	80	73	60
Diff./ $\sigma_{diff}$ .....	4.3	6.0	4.8	3.9	3.7		
<b>Interoperative tests: Second series</b>							
Number of trials.....		50	40	50	60	40	30
Per cent correct.....		96	88	88	83	70	50
Diff./ $\sigma_{diff}$ .....		5.9	4.0	4.7	4.0		

the midline through the indentation marking the superior end of arcuate, and thence onto the mesial surface to the sphenoidal ridge. The block of tissue was removed in one piece (weight 4.5 grams in the fresh state). In cleaning up the edge of the lesion, the arcuate sulcus was followed to its depth. There was no indication of injury to the premotor or motor areas, nor evidence of encroachment upon the basal ganglia. Possibly another half gram of tissue was removed in cleaning up the lesion with the sucker. Hemorrhage was slight, the field was left dry and closure followed in the usual manner.

operations when the premotor areas were removed showed that the cortex anterior to the arcuate sulcus on the mesial, dorsal and fronto-lateral surfaces of the frontal lobe had been destroyed in both hemispheres. The motor and premotor areas adjacent to the lesions were well vascularized, and biopsy examination of the premotor areas did not disclose any abnormality.

In view of S's retention of problem box habits, of the ability to respond correctly when no delay was introduced, and of the excellent motivation and orientation to general features of the training situation, it seems evident that the *failure* on the delayed response test after bilateral injury of the frontal areas represents a significant behavioral deficit. This was not overcome by training in excess of that given prior to operation. Further, this deficiency can not be explained as a generalized dementia, but it appears to be specific to delayed response.

*Experiment 4. Serial bilateral extirpation of frontal areas.  
(Frontal V)*

The subject of the experiment was a vigorous and active immature white crown mangabey monkey (*Cercocebus torquatus*) which had been under observation for several months before training was undertaken. Prior to coming to the laboratory it had been a pet, and was unusually friendly and well adapted to handling. Its weight was 3000 grams.

*Preoperative training.* Preoperative training included experience with various puzzle boxes and extensive tests on delayed response. Detailed descriptions of problem box solutions will not be reported since these responses were not significantly altered by injury of the frontal association areas. Similar material has been published elsewhere (25).

Training in delayed response was started with delays of five seconds and with only the grille door in use. In successive ten trials, 80, 100, 100 and 90 per cent of choices were correct. Both the grille and solid doors were used on the next twenty trials. The percentage of correct responses was 90. It is significant that practically no training was required before S responded in a manner sharply differentiated from a chance performance. This ready adaptation stands in contrast with failure to adjust, in spite of long retraining, after bilateral injury of the frontal areas. The number of trials, the per cent of correct choices and the reliability of the difference between S's scores and chance values are presented in table 2. Within the limits of the training procedures employed, delays in excess of one minute were beyond the range of ability. Other significant features of behavior will be considered later.

later removed with the sucker in cleaning the edges of the lesion. There was little hemorrhage and when the field was dry, the dura was drawn over the cortex and closure effected in the usual manner.

First and second days. The animal was alert and active, it ate normally and exhibited its former interest in persons and events in the laboratory. There was no evidence of forced grasping or of diminished motor power and skill. No visual defect was found. S watched E write and when given the paper, traced the course of several curving lines with its fingers, then folded and played with the paper.

Third day. The face was edemic and slight hemi-paresis of the left side was detectable. S did not correct placing of the foot when it slipped over the edge of the table and frequently walked on the dorsum of the hand. Hemianopsia was now marked, but without the limitation of eye movements noted after the first operation. S was alert and active, explored the laboratory and played with attendants in the same manner as it had done prior to this operation.

Fourth day. Motor power of the left side was impaired and while all limbs were used in walking, the left upper extremity was not used to manipulate food. There was no forced grasping, no facial paralysis and no deviation of the tail; eye movements were normal, but the left field hemianopsia continued.

Fifth day. Motor symptoms had nearly disappeared although the hemianopsia remained.

Fourteenth day. All evidences of motor deficit had disappeared; motor power was equal on both sides, and finely adjusted movements were accomplished with ease and skill. The hemianoptic condition had not changed.

Sixteenth day. The scalp was badly lacerated and superficially infected in a fight with another monkey. The neurological picture was unchanged.

Fifth week. The scalp wound was healing slowly and since the hemianopsia had cleared up, the animal was tested on problem boxes and delayed response. It was ravenously hungry and extraordinarily active, although without change in the basal metabolic rate (8). The neurological condition of the subject continued without change until the pre-motor area of the right hemisphere was removed at a third operation.

*Postoperative tests.* Although the excision of one frontal area had not altered the subject's responses to delayed reaction tests, removal of the frontal area of the other hemisphere resulted in behavioral disturbances similar to those observed after simultaneous bilateral extirpation (ex-

By late afternoon, S took water and munched bananas. There was no forced grasping, although slight motor deficit in the right upper extremity was evident when S attempted to manipulate food. Running and climbing movements were symmetrical and motor power was normal.

First day. Motor power was definitely impaired in fingers and wrists, but without evidence of forced grasping. The eyes were deviated to the right and did not rotate beyond the midline in following moving objects. S walked in circles toward the left, apparently due to an hemianoptic defect. There was no infection or edema.

Fourth day. Recovery was excellent. Motor power was returning and the eyes, while still deviated to the left, could now be moved to the right limit of normal excursion. There was no forced grasping.

Tenth day. Motor power was equal in both extremities, although there was preferential use of the left hand for finely adjusted skilled movements. There was no hemianopsia and eye movements were normal.

Fifteenth day. S appeared quite normal in the use of the extremities, and there was no indication of visual defect. Retention tests on the problem boxes and delayed response were made at this time.

*Interoperative tests.* S was tested on problem boxes when recovery of motor power and performance seemed stationary (sixteenth day). There was no impairment of responses to these tests. (Cf. experiment 1, this paper, and (25).

The results of two series of tests, the first given three to four weeks and the second six months after operation, are summarized in table 2. Perusal of these data indicates that removal of the left frontal area had not impaired S's capacity for delayed response. In each series of tests, as in the preoperative tests, S failed when the delay exceeded sixty seconds in duration. These results stand in sharp contrast with those obtained after the lesion was made bilateral by extirpation of the other frontal area.

*Second operation.* Under sodium amytal anesthesia, supplemented with ether, a large right-sided bone-flap was turned back. A bony defect was noted at the lower anterior margin of the flap, associated with a defect in the dura, and an old, yellow gliosis of the cortex which evidently had been infected at one time. After coagulation of veins, an incision was made along the arcuate sulcus and extended over the mesial surface. The ultimate dissection was made with blunt spatulas, care being exercised to avoid the caudate nucleus. The weight of the excised tissue was 3.9 grams in the fresh state. A small amount of tissue was

TABLE 3  
Summary of postoperative tests on delayed response and training on visual discrimination. (Frontal V)

TEST SITUATION	TIME AFTER SECOND OPERATION	NUMBER OF TRIALS	PER CENT CORRECT CHOICES
Delayed response (grille only)	Fifth and sixth weeks	80	50
	Fourth month	30	*
8 cm. white square vs. black	Fifth month	1-10	50
		11-20	70†
		21-30	80
		31-40	90
		41-65	94
		66-96	100†
Delayed response‡ (grille only)	Fifth month	20	35
2 cm. white square vs. black	Fifth month	10	80
8 vs. 2 cm. white square		10	90
16 vs. 8		10	90
12 vs. 2		10	90
12 vs. 4		10	80
3 training trials 8 vs. 2 cm. square	Fifth month	35	86
Test trials			
16 vs. 12		10	70
16 vs. 4		10	100
12 vs. 4		10	90
Delayed response‡ (grille only)	Fifth month	70	47

\* Less than 50 per cent; position preference marked.

† The subject reached a criterion of 80 per cent correct in 30 trials after the fourteenth trial; of 100 per cent after the sixty-fifth trial.

‡ Several test series of ten trials on 8 cm. white square versus black and 8 versus 2 cm. white squares were interpolated between successive ten trials on delayed response. In each instance the per cent of correct choices was ninety or better on the discrimination tests.

and for interspersed tests on delayed response (grille door only in use) are summarized in table 3. Prior to training in discrimination of an 8 cm. white square versus black, S had been given 110 trials on de-

periment 1). The first tests on delayed response were carried out during the fifth and sixth weeks. Motor and sensory disturbances had entirely cleared, and S was alert and well oriented to the problem situation. It had previously shown excellent retention when tested on the several problem boxes.

As in the preoperative training, the testing was started with only the grille door in use, thus permitting S to maintain its visual orientation toward the test objects. In eighty trials, distributed over five days (table 3), S made 51 per cent of correct choices, in contrast with 93 per cent in the first forty trials of preoperative training. In these tests S was well motivated, apparently observed the loading of the cups, and showed no sustained position preference from one day to the next. Increasing the amount of food per trial and reducing the number of trials per day did not improve its performance. During the delay period and between trials S showed no greater activity than before operation, but it did exhibit a different type of activity. The spontaneous playful jumping, climbing, and chattering were to a degree replaced by the stereotyped pattern of repeatedly pacing around the cage. On the other hand, S continued to explore and take to pieces any movable parts of the apparatus and to collect nails, fruit seeds, pieces of string and other miscellaneous objects that it found when free in the room.

Training on delayed response was again undertaken during the sixteenth week. In thirty trials, S showed no evidence of improvement and exhibited a pronounced position preference for the right cup. It apparently watched closely the loading of the cups, and on ten test trials without delay,—i.e., with the grille and opaque doors raised and S permitted to approach the cups as the food was being concealed—it responded correctly each time. However, under the same conditions, the introduction of distractions such as talking to S or snapping one's fingers while it advanced toward the cups gave scores no higher than chance values.

In order to establish adequately that failure in the delayed response situation was not due to inability to attend and respond to spatially separated stimuli, training on visual discrimination was undertaken. The apparatus and training procedure are described in the section on methods; for purposes of comparison with the delayed response, it is of interest to note that the patterns to be discriminated were separated by the same distance as the cups in the delayed response test, and that in certain discriminations it was necessary for S to compare the two stimuli before making its choice. The data for visual discrimination training



acquisition. Extirpation of the second premotor area caused complete loss of problem box habits and failure, within the limits of training, to reacquire these responses. Further details of these observations will be presented in a separate report.

*Verification of lesions.* Examination of the brain *in situ* at the third and fourth operations showed that the cortex anterior to the arcuate sulcus on the mesial, dorsal, and orbital surfaces of the frontal lobe had been destroyed in both hemispheres. Biopsy examination of the pre-

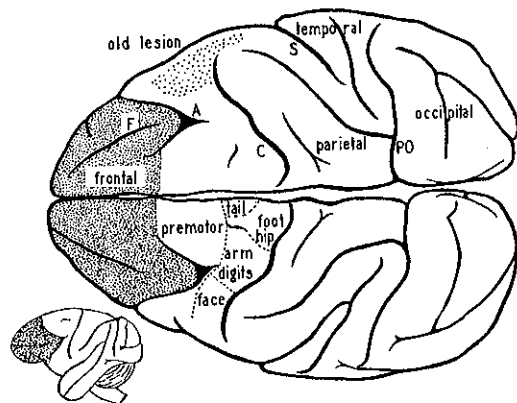


FIG. 3. CAMERA DRAWING OF THE BRAIN (EXPERIMENT 2), SUPPLEMENTED FROM CELLOPHANE TRACINGS MADE AT OPERATION, SHOWING THE LOCUS AND EXTENT OF THE EXPERIMENTAL LESIONS OF THE FRONTAL AREAS (HEAVY STIPPLING) AND AN OLDER INJURY AND SCAR FORMATION (LIGHT STIPPLING)

The electrically excitable regions for leg, arm, and face are indicated.  $\times 1$

motor areas indicated normal appearing tissues. The loci and extent of the several lesions are represented diagrammatically in figure 3.

#### Experiment 3. Subtotal extirpation of the frontal areas. (Frontal IX)<sup>3</sup>

The subject of the experiment which involved extirpation of the left frontal area and several months later partial excision of the right, was an immature male baboon (*Papio papio*). Its weight was 6000 grams.

*Preoperative training.* In view of the disturbance of delayed response

<sup>3</sup> The effects of subtotal lesions are not adequately treated in this experiment. In cooperation with Drs. Haslerud and Taylor the writer is studying a series of animals with subtotal, bilaterally symmetrical lesions.

layed response with less than fifty per cent of successes. By the fourteenth trial on the visual discrimination problem S reached a criterion of 80 per cent correct in thirty trials and of 100 per cent by the sixty-fifth trial. Learning of the problem to the 80 per cent criterion was about the same as that of two normal animals; to the 100 per cent criterion, it was slower and suggests that distractibility may have been greater after frontal injury. Ten trials on delayed response, 30 per cent correct, ten trials on 8 cm. square versus black, 100 per cent correct, and ten trials on delayed response, 40 per cent correct, followed. On delayed response there was a strong left preference that was not detectable during the discrimination tests.

In order, ten trials on discrimination of 2 cm. white square versus black, 8 versus 2 cm. white square, 16 versus 8, 12 versus 2, and 12 versus 4 with scores better than 80 per cent in each ten trials were given. In the next series of tests, three trials on 8 versus 2 cm. white square were followed by one trial on each of three pairs—16 versus 12, 12 versus 4, 16 versus 4—presented in an irregular sequence. Seventy additional trials on delayed response gave but chance scores. The high percentage of correct responses and the frequent comparison of stimuli before choice indicate that S was able to attend and respond differentially to spatially separated stimuli. Retention tests on the various problem boxes were repeated at the completion of the visual discrimination and delayed response tests (five months after operation). They revealed no impairment of either memory or motor skill.

The deficit following bilateral extirpation of the frontal areas, *seriatim*, is not indicative of a general dementia, but points to failure which is specific to certain aspects of behavior. Thus, S was able to attend and respond with a high degree of success in situations in which the differential cues were present in the sensory world (visual discrimination, simple problem boxes, and in the delayed response situation *when the response was made without interposition of delay*) but it failed in those situations in which the differential cues could operate only through retention and recall from earlier experience (delayed response and certain aspects of serial problem boxes).

*Subsequent history.* At the completion of the above tests, the animal was subjected to two operations at which the left and right premotor areas were successively removed. There was no change of status with respect to delayed response. Following extirpation of the left premotor area, there was serious impairment of memory for the several problem box habits. Relearning required slightly longer than initial

TABLE 4

Summary of pre-, inter-, and postoperative tests on delayed response, showing number of trials, per cent of correct choices, and reliability of the difference between the obtained values and the assumed chance value of 50 per cent  
Delay periods between five and one hundred eighty seconds. (Frontal IX)

	PERIOD OF DELAY IN SECONDS									
	5	10	15	20	30	45	60	90	120	180
Preliminary training (grille only)										
Number of trials.....	90	10		10	10		10		10	
Per cent correct.....	89	90		100	100		100		90	
Preoperative tests										
Number of trials.....		30			30	30	30	40	40	
Per cent correct.....		90			97	90	80	73	53	
Diff./ <i>caut.</i> .....		7.3			13.2	7.3	4.1	3.3		
Interoperative tests										
Number of trials.....		30			40	50	50	40	40	40
Per cent correct.....		97			87	88	88	80	73	60
Diff./ <i>caut.</i> .....		15.2			7.7	8.3	8.3	5.3	3.3	
Postoperative tests										
Number of trials.....	45	10	25	Two weeks after second operation						
Per cent correct.....	82	60	48	Grille door only						
Number of trials.....	60			Three months after second operation						
Per cent correct.....	75			Grille door only						
Number of trials.....	45	35	20	Three months after second operation						
Per cent correct.....	65	60	50	Grille and solid doors						
Number of trials.....	40	40	40	Seven months after second operation						
Per cent correct.....	75	57	55	Grille and solid doors						
Number of trials.....	80			As above						
Per cent correct.....	81									
Number of trials.....	10	10	10	Test trials after eighty training trials						
Per cent correct.....	70	60	50	at five second delays						
Number of trials.....	175	85	70	Total of all trials in which grille and solid doors were used						
Per cent correct.....	75	59	53							
Diff./ <i>caut.</i> .....	4.9	1.5	0.5							

shown in experiments 1 and 2, it seemed desirable to determine more carefully S's ability to delay with only the grille door in use as well as with the solid door. The results of preoperative training are presented in table 4. It is evident that with only the grille door in use S responded successfully after delays of at least two minutes. The first series of tests with the solid door in use showed better than chance scores with delays up to ninety seconds.

*Operation and recovery.* Under sodium amytal anesthesia a left bone-flap was elevated, the dura reflected, and the cortex mapped on cellophane. Extirpation of the left frontal area was effected by making an incision slightly anterior to the arcuate sulcus in order to avoid disturbing a vein which drained the motor and premotor areas. The incision was then extended to the mid-line and to the lateral and orbital surfaces by means of spatulas. The excised tissue weighed 6.7 grams and in addition one or two grams of tissue were removed with the sucker. Closure was completed in the usual manner.

Recovery was uneventful; there was no disturbance of either motor power or skill, and no indication of hemianopsia. Retention tests were begun three weeks after operation.

*Interoperative tests.* Twenty preliminary trials with only the grille door in use resulted in 90 per cent correct choices after delays of five seconds. The results of the regular series are summarized in table 4. It is clear that excision of the left frontal areas produced no impairment of capacity for delayed response.

*Second operation.* A right bone-flap was prepared and after making a cellophane tracing, the frontal areas were incised with the Davis-Boyd unit about 1 cm. anterior to the arcuate sulcus. The incision was then carried downward by means of spatulas and the anterior portion of the frontal area removed in one piece (weight 4.5 grams). Closure was effected in the usual way.

There was no evidence of sensory or motor deficit at any time after the operation. The animal was alert and active, and explored objects and persons with its usual energy.

*Postoperative tests.* Retention tests were undertaken between the tenth and fifteenth days after operation. The results, summarized in table 4 indicate serious impairment of capacity for delayed response. Thus S made scores significantly better than chance with only the grille door in use after delays of five seconds, but it failed when the delay period exceeded this value. In twenty trials with both solid and grille doors in use, S made 45 per cent correct choices after five to ten seconds of delay.

to explore the effects of subtotal lesions, it was decided to sacrifice precise knowledge of the second lesion in order to determine whether capacity for delayed response would be destroyed if the lesion of the frontal area was made bilaterally complete. During the six weeks that S survived after this operation, there was no indication that it was able to respond in better than a chance manner to the delayed response tests. Death occurred from pneumonia before completion of these tests.

*Verification of lesions.* The approximate boundaries of the lesions are shown in figure 4. In the left hemisphere the lesion involved all of the frontal area except a few millimeters of tissue anterior to the inferior limb of arcuate sulcus (eye-fields). The lesion in the right hemisphere was less extensive and involved chiefly the frontal pole. A band of tissue about one centimeter wide and lying anterior to the arcuate sulcus, was found to be normal at biopsy examination after the third operation. The posterior limits of the lesion, as indicated in figure 4, are estimated from cellophane tracings and autopsy examination.

*Experiment 4. Serial bilateral extirpation of the parietal region.*  
(Frontal VIII)

The subject of the experiment was an immature male mangabey monkey (*Cercocebus torquatus*) which had been under observation for several months before training was begun. Its weight was 4100 grams.

*Preoperative training.* Preoperative training included experience with various problem boxes, visual discrimination, and delayed response. Significant features of the results will be considered in relation to postoperative performances.

*Operation.* Under sodium amytal anesthesia, a large left bone-flap was turned down, the dura reflected and the chief markings traced on cellophane. The lesion was made with the Davis-Bovie knife by coagulating the veins draining the area to be extirpated and then incising the margins of the lesion. The tissue between the intraparietal and the parieto-occipital sulci was removed; the portion of the parietal association area lying on the mesial surface was not included in the extirpation. Closure was effected in the usual manner.

*First day.* S was alert and active, but it showed evidence of sensory deficit. The right arm and leg were extended and were not corrected for abnormality of posture; walking was accomplished with a wide base on the affected side. There was turning and rotation on the longitudinal axis, and S definitely sought contact with the walls of the cage or some object in the room. Pinching the dorsum of the foot elicited a vigorous

Testing was deferred until the twelfth week to permit further recovery. At that time S made 75 per cent correct choices after delays of five seconds with only the grille door in use. With both grille and solid doors in use performance was but slightly better than 50 per cent after delays of five, ten and fifteen seconds. Seven months after operation, forty trials with delays of five, ten and fifteen seconds indicated some success after delays of five seconds but failure when the delay exceeded this value. Eighty training trials (five second delays) were then given

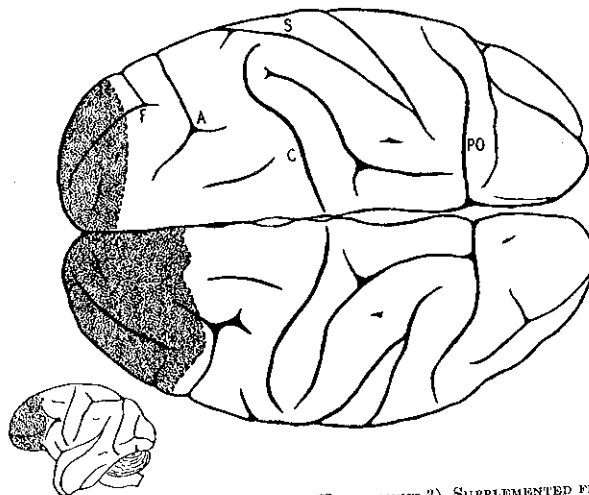


FIG. 4. CAMERA DRAWING OF THE BRAIN (EXPERIMENT 3), SUPPLEMENTED FROM CELLOPHANE TRACINGS MADE AT OPERATION, SHOWING THE APPROXIMATE BOUNDARIES OF THE LESIONS.  $\times 1$

with a score of 81 per cent correct. However, performance after delays of ten and fifteen seconds had not been improved by this training. Summarizing all postoperative trials on which the grille and opaque doors were used it is noted that the percentage of correct choices after delays of five seconds was distinctly above chance expectations. On the other hand when delays exceeded this value, accuracy was not reliably better than chance.

*Third operation.* Since the primary purpose of this experiment was

TABLE 6  
Summary of training and postoperative testing on visual discrimination.  
(Frontal VIII)

TEST SITUATION	NUMBER OF TRIALS	PER CENT CORRECT CHOICES
Preoperative tests		
8 cm. white square vs. black	1-10	50
	11-20	20
	21-30	60
	31-40	80
	41-50	80
	51-60	100
	61-70	80
	71-100	100
3 training trials		
8 vs. 2 cm. white square	66	94
Test trials		
16 vs. 12	20	75
16 vs. 4	20	90
12 vs. 4	20	90
Interoperative tests		
8 cm. white square vs. black	30	97
Postoperative tests		
8 cm. white square vs. black	30	100
Various*		
8 vs. 2	5	100
4 vs. 2	5	100
12 vs. 4	5	100
16 vs. 8	5	100
12 vs. 8	5	100
16 vs. 12	5	80
8 vs. 4	5	100
12 vs. 8	5	100
16 vs. 12	10	50
8 vs. 4	5	100
12 vs. 8	10	90

\* The various pairs of stimuli were presented in groups of five trials. Each succeeding pair followed immediately upon completion of the preceding test. The line indicates a break of twenty-four hours.

response after a delay of one or two seconds. Light stroking of the skin or pulling the hair failed to evoke a reaction until S saw its hand being held by the experimenter, after which it quickly withdrew its hand. There was complete hemianopsia of the right visual field. The pupils were equal and extraoptic movements were normal.

Fourth day. S corrected abnormal positions more readily and seemed more responsive to light touch although the reactions continued to be slower than on the side homolateral to the lesion. Hemianopsia remained unchanged.

TABLE 5  
Summary of preoperative, interoperative and postoperative tests on delayed response showing the number of trials, per cent of correct choices, and reliability of the difference between obtained values and the assumed chance value of 50 per cent. Delay periods between fifteen and one hundred twenty seconds. (Frontal VIII)

	PERIOD OF DELAY IN SECONDS					
	15	30	45	60	90	120
Preoperative tests						
Number of trials.....	115	60	80	80	60	
Per cent correct.....	92	87	76	70	60	
Diff./chance.....	7.9	5.8	3.5	2.6		
Interoperative tests						
Number of trials.....	30	30	40	40	30	
Per cent correct.....	97	87	90	80	50	
Diff./chance.....	5.5	3.4	4.3	2.9		
Postoperative tests						
Number of trials.....	40	40	30	30	30	20
Per cent correct.....	93	85	83	92	73	60
Diff./chance.....	4.9	3.6	2.9	4.1		

Tenth day. The extremities were used well in climbing, and the disturbances of motor performance that could be detected appeared to be of sensory origin. Hemianopsia was complete to the midline; threatening or the offer of food in the blind field elicited no reaction.

Four weeks. The extremities were used with a considerable skill for walking and for finer manipulations although the left hand was preferred whenever possible. Sensory symptoms had largely abated, the right field hemianopsia had cleared up and S seemed ready for retention tests.

placed in its hand, although it had not been able to grasp the sugar lump initially with that hand. It was still ataxic, but walked and climbed quickly and accurately. No difference in touch or pain could be detected between the two sides.

Two months. S showed marked improvement in motor performance although there was still some inaccuracy in executing finer movements of the fingers. Walking and feeding were accomplished without difficulty. There was still some evidence of disarticulation of visual and kinesthetic space as seen in the past pointing when reaching for food,

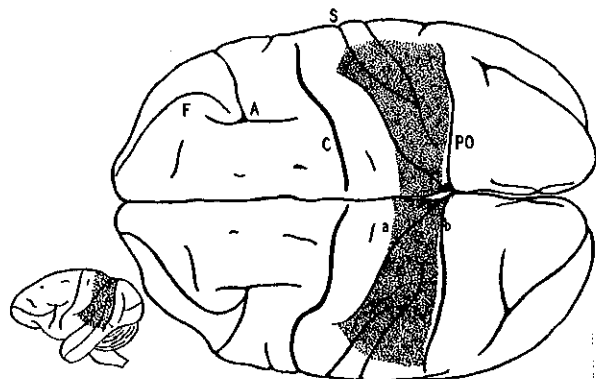


FIG. 5. CAMERA DRAWING OF THE BRAIN AT AUTOPSY (EXPERIMENT 4) SUPPLEMENTED FROM CELLOPHANE TRACINGS MADE AT TIME OF OPERATION

The boundaries of the lesions were verified from histological examination.  $\times 1$ .

and in the tendency to bump into objects, e.g., table legs or the partitions in the training cage. This defect was not readily attributable to visual defect *per se* since the accuracy of visual discriminations had not been impaired by these lesions.

*Postoperative tests.* Performance on problem boxes was slower and more clumsy than it had been in the preoperative training period. The defects noted were of a sensory nature, and there was no suggestion of impairment of the pattern of response as has been noted after lesions of the premotor areas (26). Inspection of table 5 clearly indicates that the bilateral extirpation of the parietal association area had not impaired the

*Interoperative tests.* The motor performance had not been greatly impaired by the parietal lesion, and such changes as were necessitated by the right hand preference were readily made. The results of the interoperative tests of delayed response are summarized in table 5. It is evident that unilateral injury to the parietal association area had not significantly altered the level of performance. The interoperative tests on visual discrimination are summarized in table 6. Excellent retention of black-white discrimination is indicated; size was not tested. The speed with which the subject reacted was consistently slower than in the preoperative training. Change in time of reaction was not noted on the delayed response tests.

*Second operation.* The procedure described for the first operation was followed in making a lesion in the right parietal region.

First day. S was in good condition although quiet. There was pronounced ataxia of the extremities of the left side, and S failed to correct abnormal postures of the limbs. Ataxia was also present on the right side but in lesser degree. Small objects could be grasped and the animal fed itself, but only with guidance of visual cues. Touch was seriously impaired on the left but it appeared normal on the right side. A pronounced left-field hemianopsia was present; vision in the right field was good.

Second day. Sensory deficit was great; S was ataxic and failed to correct abnormal postures. Two or three attempts were often made before success in grasping bits of food, and S was guided by visual rather than by kinesthetic cues. If S's attention was distracted in the midst of reaching for an object, its hand went wide of the mark by several centimeters, generally with the fingers hyperextended. At times S dropped the food but completed the movement to the mouth apparently unaware that the food had been lost. Hemianopsia persisted and the animal turned constantly to the right.

Third day. There was no significant change from the preceding day.

Seventh day. S stood and walked adequately. It was still ataxic and movements seemed to be guided by visual cues. Rather unsuccessful attempts were made to manipulate food with the left hand. Tactile sensitivity on the left had greatly improved.

Two weeks. Past pointing to the right continued when S grasped for food, and as before, visual cues were predominant in regulating directed movements. The hemianopsia had disappeared and the motor performance, apart from sensory deficit, was improved. S transferred a sugar lump to its mouth with the left hand after the piece had been

delayed response or, at best, made inferior performances under simplified conditions. However, by the seventh month S responded correctly after delays of five seconds but failed with longer delays. Comparison with preoperative performance and with tests after the extirpation of one frontal area (delays were longer than ninety seconds) shows profound deterioration after partial destruction of the second frontal area. It should be noted, however, that this partial lesion did not completely abolish capac-

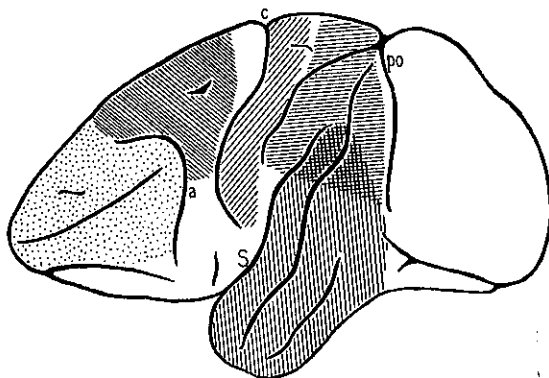


FIG. 6. SCHEMATIC SUMMARY OF THE EFFECTS OF CORTICAL ABLATIONS ON CAPACITY FOR DELAYED RESPONSE

Extirpation of the variously hatched regions—parietal, postcentral convolutions (2), temporal lobes (29) and motor-premotor areas (30)—caused no impairment of ability. Ablation of the stippled area was followed by permanent impairment of capacity for delayed response. Later experiments with small lesions of the frontal lobe indicate that the essential region for delayed response is restricted to a small area about the frontal sulcus.

ity for delayed response but reduced the length of the delay period.

Retention and execution of two other problem solutions—visual discrimination and simple puzzle boxes—were not significantly altered by either unilateral or bilateral ablation of the frontal areas. (See an earlier and more extensive report by the writer (25) in addition to the present observations.)

*Other cortical areas.* In order to establish dependency of de-

performance on the delayed response tests either in accuracy or in length of delay. If one were to ascribe any difference to the several performances, he would be forced to conclude that the subject had improved after bilateral extirpation of the parietal association areas. The results of the postoperative tests of visual discrimination are presented in table 6. Inspection shows no significant change in the accuracy of discrimination after bilateral injury of the parietal association areas. The slowness of reaction in the visual tests, noted after the first operation, was also observed in these tests. It was the only significant change revealed by any of the several tests used in these experiments.

*Verification of lesions.* The extent and loci of the lesions are indicated in figure 5. Examination of the brain showed that the cortical tissue between the parieto-occipital sulcus and the interparietal sulcus had been destroyed with the exception of a band, a few millimeters wide, on the anterior surface of the parieto-occipital fissure. The lower boundary extended from the end of the parieto-occipital fissure to the lower limit of the interparietal and thus included the upper part of the first and second temporal gyri. The anterior limit was formed by the lower part of the interparietal sulcus as far as the point where this sulcus flexes caudally; from this point the lesion extended to the mid-line. The mesial aspects of the hemispheres were not involved.

#### DISCUSSION

##### *Summary of results*

The results of the several experiments are summarized graphically in figure 6. Brief recapitulation of the findings will be given.

*Frontal association areas.* Unilateral extirpation of the frontal association area resulted in no impairment of delayed response as indicated by either length of delay or accuracy of performance (experiments 2 and 3). However, when the lesions were extended to include the frontal areas of both hemispheres, total and permanent loss of capacity for delayed response ensued. This occurred when the frontal areas were removed simultaneously (experiment 1) and *seriatim* (experiment 2).

In experiment 3, the left frontal area was removed completely without interfering with capacity for delayed response, and at a later time the anterior half of the right frontal area was ablated. For several months following the second operation, S failed on

be given. (a) *The frontal association areas do mediate a type of behavioral adaptation which the organism is incapable of exhibiting in the absence of this region.* Destruction of the frontal areas is followed by failure to adjust to the delayed response tests. Complete bilateral destruction does not merely lower the efficiency of performance but totally abolishes capacity for such behavior. Furthermore, this loss, within the limits of postoperative training employed in these experiments, is a permanent deficit. In a series of related studies on the delayed alternation problem (Jacobsen and Nissen, 31) as many as two thousand postoperative trials have been given without indication that the subjects profited from such experience. The conclusion seems justified that destruction of the frontal areas is followed by profound and permanent deterioration of certain types of behavioral adaptation. (b) *This contribution is peculiar to the frontal areas; similar behavioral deficits do not follow equally extensive injuries in other parts of the cortex.* Extensive injury in other regions causes no deterioration of delayed response capacity. The deficit which follows frontal injury is specific to lesions of these areas. Anatomical and functional specialization of the motor and sensory projection systems in the primate brain has in the past been clearly recognized. The significance of the present experiments lies in the demonstration that not all parts of the cerebral cortex in primates are functionally equivalent at more complex levels of organization, but that here also there is specialization within restricted regions. In this respect our results are in agreement with Poliak's anatomical findings and deductions. He writes:

"... the present investigation points to a division of the cerebral cortex into receptor fields and intercalated or association areas or regions, approaching in this respect the conception of Flechsig, supported by Henschen and a number of other neurologists, although their conceptions must be modified somewhat. There is another related question which must, however, be settled by physiological experiments and by clinical studies. Are the projection areas to be regarded exclusively as 'gateways' of the cerebral cortex for incoming impulses, comparable to the switchboard of a telephone station, as claimed by Flechsig and Henschen, or, do they participate likewise in higher integrative processes, as

layed response upon the frontal association areas, it is necessary to show that extensive ablations in other cortical regions cause no deterioration of this ability. Results will be summarized for experiments treating the parietal, postcentral, temporal and precentral regions.<sup>4</sup>

Unilateral, and later bilateral, extirpation of the *parietal* areas caused no alteration in either accuracy or level of performance on delayed response (experiment 4). Jacobsen and Elder (29) have reported that neither unilateral nor bilateral extirpation of the *temporal* lobes influenced level or accuracy of performance on delayed response. The effect of removing the *postcentral convolutions* has been studied by Breslow, Barraro and Warden (3). They report no deterioration of delayed response ability after unilateral and bilateral injury. Invasion of the *motor* and *premotor* areas constitutes a severe test of the point in question since it involves tissue adjacent to the frontal areas and seriously interferes with the postural and locomotor mechanisms. It is significant to note in the case reported by Jacobsen and Haslerud (30) that motor performance was so impaired that the experimenter had to open the food containers after S had indicated its choice by touching one of them. However, accuracy of performance was in no degree impaired and the length of delay period was slightly greater after operation than before. This improvement probably resulted from better emotional adjustment.

#### *Localization versus equipotentiality*

In formulating the problem of these experiments two neurologically directed questions were asked to which answers may now

<sup>4</sup> The present techniques are not suited to investigation of the effects of extensive injury to the visual areas. After occipital lobectomy in monkeys, response to photic stimulation, except for pupillary reflexes and conditioned responses to brightness, is lost (48, 49), and response to other modes of stimulation is seriously disrupted by the visual defect. For present purposes, however, the visual areas may be tentatively excluded as a region efficacious in mediating delayed response since in experiments 1, 2, and 3 extensive training did not restore capacity for delayed response although the occipital region was intact. Observations made in connection with other experiments in which small scattered lesions were produced in the peripheral projection region and in the visual association areas showed no impairment of delayed response.

point toward a different plan of organization in the primate brain, an organization in which specialized association areas mediate the more complex integrative functions which are subserved in the rat by the cortex as a whole.

In comparing rodent with primate, it is necessary to establish as well as possible the functional equivalence of the several tests used for the two types of subjects. Methodologically the delayed alternation problem closely parallels delayed response. Loucks (43) has reported a correlation of  $+ .54$  between extent of lesion and degree of deficit as measured by postoperative relearning of the delayed alternation habit. Unfortunately data are available for only the frontal region of the rodent cortex. Maier's (46, 47) experiments with "reasoning" tests provide data for the frontal and occipital portions of the cortex. From an analysis of his experimental procedures, enough common features are found in the delayed response and "reasoning" problems to permit comparison of results from these techniques. The task confronting the rat is to make a correct choice between the paths leading to two tables on one of which the animal had been fed a short time previously. It is evident that whatever other factors may be involved, such as spatial orientation, capacity for recent or immediate memory is essential to the solution of the problem.

This factor then is common to the "reasoning" and delayed response tests. (Maier (45) has indeed used the "reasoning" problem to study delayed response as a phenomenon of memory.) Neurological results show rather close correspondence between extent of lesion and degree of behavioral deterioration:  $r = + .54$  and  $+ .75$  for the frontal and occipital regions respectively.

More adequate data are found in the maze studies of Lashley (34) and Lashley and Wiley (41). Lashley reported more or less severe deterioration on each of three inclosed mazes. Mazes I and II were a simple T-maze and a slight modification of the T-maze respectively; they required no great amount of patterning of behavior and were relatively resistant to cortical injury. Maze III was a shuttle type of maze which required the animal to establish the habit of alternately turning right, left, right and left at successive choice points. Lashley's analysis indicates that

assumed by other neurologists (Nissl von Mayendorf), thus depriving the intercalated regions of the exclusive monopoly of these higher processes?" (52, pp. 212-13).

It goes beyond the present experiments to attempt to answer completely the several problems raised by Poliak. However, the experiments do demonstrate that for at least one type of complex behavioral adaptation, and we believe for others also (28), the frontal association areas have exclusive control, and in the absence of these areas, no other regions—sensory, motor or association—are capable of mediating those functions.

The present experiments avoid certain criticisms (see p. 15) which have been justly directed against earlier experiments and clinical studies by both parties to the localization controversy. In the present experiments the ablations were complete, hence the differential effects on delayed response and on other problems can not be dismissed on the basis of inadequate surgical lesions. On the other hand, equally extensive injuries have been produced in other cortical regions without significantly altering performance on the test which was severely disturbed by injury of the frontal areas. Comparison of pre- and postoperative behavior is not impressionistic, but is based on results from controlled test situations. Furthermore, postoperative tests were made not only within a few weeks following operation but after many months during which the subject received postoperative training. Hence the behavioral loss is not a transient disturbance due to operative shock or diaschisis but represents a permanent residual deficit. Additional control of operative shock is found in cases of unilateral frontal lesions and of injuries to other parts of the cortex.

#### *Comparison of rodent with primate*

Reference has been made in a previous section to the existence in rodents of two distinct types of organization within the same cortical area: one in which the differentiated structure was predominant (vision) and another in which the undifferentiated mass of tissue was of greater importance than the mosaically localized elements (maze learning). The results of the present experiments



brought out by the maze and "reasoning" techniques and by the delayed response tests, it then is evident that a different plan of cortical organization prevails in the primate brain than in the rodent. It would thus appear that behavioral adaptations which depend on or utilize in some manner the capacity designated above as immediate memory depend on special association areas in the monkey but on the cortical mantle as a whole in the rat.

This distinction between primate and rodent is in harmony with the available anatomical data. Brodmann (5) suggests that frontal tissue, if present at all in the rodents, is of a primitive character. Anatomically he has traced the increase in frontal tissue through several orders of mammals and has given the following indices of the proportion of frontal cortex to total cortex: hedge-hog, 0 per cent; rabbits, 2.2 per cent; cat, 3.4 per cent; dog, 6.9 per cent; macaque, 8.3 per cent; capuchin, 9.2 per cent; gibbon, 11.3 per cent; chimpanzee, 16.9 per cent; and man, 29 per cent. On the behavioral aspect, little precise information is available except for the rat and primates. Removal of the frontal areas in dogs is known to produce increased activity similar to that observed in primates, but careful study of complex behavior is lacking. Among the primates, it is evident that the behavioral disturbances are more varied in chimpanzee (28) than in monkey, and only in the former do the emotional disturbances stressed by Feuchtwanger (15) approach the condition observed in man after frontal injury.

While it is thus possible to indicate that a different plan of organization prevails in the cerebral hemispheres of the monkey than in those of the rat, the present experiments tell little of the functional conditions within a specialized region such as the frontal areas. It would be quite incorrect to regard them as disproving such principles as omnivalence and mass function. It may be that within a specialized area such as the frontal the component parts are functionally equivalent and that within this area, the principles of omnivalence and of mass function which characterize the cortex as a whole in the less developed organism, also characterize the activities of this specialized region in the more highly evolved cerebrum. The question is beyond the scope

the most important factors in the maze habit are a generalization of direction from specific turns of the maze and development of some central organization by which general direction can be maintained in spite of variations in posture and in specific direction of running. In the shuttle maze, the cue probably is not merely the visual appearance of the successive choice points but, at least in part, recall of the direction of the preceding turn. Lashley's discussion of the nature of deterioration after cerebral injury points to such a factor; he writes:

"One does not realize the meaning of 'random' behavior until he has compared a normal animal with one having extensive cerebral destruction. The normal animal almost never re-enters a cul-de-sac without intervening exploration of other parts of the maze. An animal with severe lesions may repeat a single error as many as two hundred times before passing to other parts of the maze. Such difference can only mean that the normal animal possesses something like an immediate memory which prevents him from repeating an error just made. Similarly after the first trial or two the normal animal gives evidence of a general orientation which the operated case is sometimes slow in acquiring" (34, p. 138).

The behavioral deficit exhibited by rats with extensive cortical injuries is strikingly similar to the defect of recent memory described in the monkey after ablation of the frontal association areas. While loss or weakness of immediate memory can not be regarded as the only factor contributing to inferior learning in rats with cortical injury, it is clear from the nature of the defect that capacity for recent memory plays an important rôle. In their several studies Lashley and Wiley have reported coefficients of correlation ranging from +.51 to +.86 between extent of cortical injury and various measures of learning and retention of maze habits. Lesions involved all parts of the neo-cortex, and within limits the several parts of the cortex appeared to be equally capable of mediating the behavior in question. Final efficiency of learning was predominantly determined by the mass of intact tissue rather than by the locus of that tissue.

If one grants a functional equivalence between the basic defects

acquisition and daily performance of habits exhibits certain deviations. Thus in discrimination and puzzle box learning behavior tends to be stereotyped; the operated animal repeats errors in contrast to the more varied behavior of the normal. Similarly, when a particular problem has been mastered, performance may be more variable. The operated animal seems more distractable in contrast to the sustained directed behavior of the normal subject. Behavior, instead of being directed by a balance of immediate, recent and temporally remote stimulation, is dominated by present external stimuli and the stable habit systems derived from earlier training; the mnemonic influence of immediately past experience is lacking. The animal without its frontal areas no longer appears to "worry" over mistakes. Whereas the normal monkey or chimpanzee may become excited, cry and have a temper tantrum, or on the other hand, turn away and ignore the problem after several successive failures, the subject lacking frontal areas seems quite impervious to any frustrating effects of errors.

In a sense the results seem almost paradoxical. The animal without the frontal association area learns and retains sensory-motor habits and visual discriminations but it is unable to remember for even a few seconds under which of two cups a piece of food had been concealed. Our difficulty, however, may arise, as Lashley (35, 39) has experimentally demonstrated, from the possibility that memory is not a unitary process but that it comprises different processes mediated through different neurological mechanisms. In support of this view Lashley has advanced data on rats which show that in discrimination learning in which the terms are so arranged as to involve only the relation of contiguity, there is little retardation in the rate of forming associations after extensive decerebration. Observations on the double latch box problem indicate that this habit may be acquired in nearly normal fashion after injury to any part of the cortex in amounts up to 58 per cent. Yet these same lesions cause retarded acquisition and impaired retention of maze habits. Maier's studies of the effects of cortical injury on learning (habit formation through repeated trials) and on "reasoning" point to the discreteness of these types of behavioral modification.

of this paper, but an affirmative answer seems to be indicated. Limited evidence from the partial lesions of the present experiments, from Harlow's observations on expanding lesions, from experiments on chimpanzee (28), and from clinical studies, shows that some degree of function is possible providing a certain minimum of frontal tissue remains intact. Experiments now in progress with the collaboration of Drs. Haslerud and Taylor suggest that the extent of lesion in the frontal lobe places a definite limit on the level of function attainable after operation.

*Considerations for psychology: Nature of the deterioration*

Bilateral injury of the frontal association areas in primates results in severe deterioration of certain modes of behavior. More specifically, operated animals are unable to remember after a lapse of a few seconds under which of two cups food is concealed. Again, if a frontally lobectomized chimpanzee is confronted with the task of getting a piece of food slightly beyond its unaided reach, it seizes and uses the nearby stick to draw in the food. Furthermore, it is able to employ a stick, too short in itself to reach the food, in order to secure a longer stick with which the lure can finally be obtained. In these problems food and stick are both present in the visual field. When the task is complicated by showing the animal a stick at one end of the cage while food is placed at the opposite end, it is not able to solve the problem. It apparently fails to remember while looking at the food that a suitable stick is available at the other end of the cage. It is as if "out of sight, out of mind" were literally applicable. The temporal organization so characteristic of normal behavior is greatly reduced, if not entirely lacking.

Deterioration, however, is not generalized; the loss is specific rather than global. Acquisition of conditioned reflexes, discrimination habits and puzzle box solutions is not significantly different (judged by trials required for learning) from that of normal subjects. Moreover, retention of such habits, acquired before operation, is not impaired by injury of the frontal association areas. Yet there is indication that although the final products tend to be equivalent to the normal, behavior during

and also in the intermediate zone between motor and frontal association areas. Furthermore it is evident that not all parts of this motor region are functionally equivalent for the intermediate zone is seen to exert a controlling and regulatory influence in relation to the adjacent motor area. It is concerned, as evidenced by stimulation and extirpation experiments, with mediation of complex patterns of movement rather than with the contraction of small discrete groups of effectors as in the case of the more readily excitable motor area. In man this type of organizing and patterning activity is most advanced and the anarthric and apraxic disturbances of speech and complex movement, associated with pathology of this region, give further insight into its functional characteristics. Attribution of a synthesizing, or serializing rôle to the frontal lobes as a whole, a point of view notably advanced by Bianchi and concurred in by later investigators, seems well founded. The results of the present experiments are in agreement with this general characterization of frontal lobe function.

It is questionable, however, whether such notions as synthesis, serializing, and organization are not too broad to be of analytical value. When a chimpanzee, although lacking its frontal areas, uses a series of three or four successively longer sticks to obtain a piece of food or learns to operate a series of levers in a definite order, or when a monkey learns a discrimination problem, behavior certainly manifests a quality describable as "synthesis." Although modified by removal of the frontal tissue, efforts of adaption are not chaotic. Synthesis or organization is clearly not a property peculiar to the frontal lobes or even the cerebral cortex. One recalls in this connection Hughlings Jackson's admonition not to inquire—"how is general mind damaged?"—but to ask rather—"what aspect of mind is damaged?" Thus, while we may grant synthesizing functions to the frontal area, our problem now becomes one of stating under what conditions and in what kind of problems, synthesis, or preferably behavior, is disrupted and ineffectual.

The present experiments suggest a definite although restricted answer. Adaptation is inadequate in those situations which

The problem, however, is not new, nor is it peculiar to animal experiments. The variety of terms used to designate the phenomena of learning and memory in man—intentional versus incidental learning, immediate memory versus more permanent retention, logical memory, memory span, recall, reproductive and associative memory—points to a similar dilemma. In a recent discussion McGeoch (50) has emphasized the need for further experimental analysis of the apparent gap, as revealed by behavioral studies, between the phenomena of the memory span and of learning by repeated trials. The present experiments at once suggest that this gap may be more real than fortuitous in that it may arise, not from incomplete psychological analysis, but from the fact that two discrete processes, mediated through different neurological mechanisms, are being studied. The several problem boxes and visual discrimination tests favor establishment of stable sensory-motor habits by repeated trials. On the other hand, the delayed response test makes quite different demands and is suggestive of the kind of events which in man we characterize as immediate memory.<sup>5</sup> These experiments can only suggest an answer to our question since more complete data on the behavioral aspect and further study of the physiological mechanisms of these phenomena with a greater range and variety of test situations are required.

Clinical interpretations of the deficit associated with pathological conditions of the frontal lobes have centered about the concept of synthesis and organization of behavior, particularly in its more complex aspects. The motorial nature of the frontal lobes has been recognized since the early clinical observations of Hughlings Jackson, clearly in the readily excitable motor area

<sup>5</sup> In using the term immediate memory to designate the defect that follows injury to the frontal areas we do so with little assurance that it is either sufficiently inclusive or descriptively adequate for the phenomena in point. In some respects recognition memory and recall appear to be better suited. It is obvious that use of any of these terms adds little to our understanding of the essential physiological and psychological problems beyond a comfortable feeling of familiarity. For the present operational definition of the functions involved may be a more satisfactory procedure.

sensory environment, and the integration and organization of recalled elements with the organism's stable habit systems.

Comparison of these complex behavioral integrations in monkey and man, is, in contrast to the simpler sensory and motor functions, particularly difficult since in the latter language mechanisms play an as yet incompletely understood part. Nevertheless the similarity and equivalence of defects seem far greater than the discrepancies. This evaluation has been kept at a minimum in this monograph until the studies on partial lesions of the frontal area in monkeys and the experiments on frontal lobectomy in chimpanzee—which, possessing a richer emotional expression than the monkey, exhibits defects that more nearly approach the behavioral deterioration seen in man—have been made available.

#### SUMMARY

The rôle of the frontal association areas in mediating complex adaptive behavior has been studied in lower primates. Monkeys were trained on two types of behavioral tests: (a) situations in which the essential cues were available in the subject's environment at the time of response (problem box and discrimination habits), and (b) situations in which certain essential cues had to be recalled from recent experience (delayed response). Experimental lesions were then made in various areas of the cerebral cortex and the ensuing disturbances analyzed. The results may be summarized as follows:

1. Unilateral lesions caused no impairment of performance on any tests. There was no evidence of hemispherical dominance.
2. Bilateral lesions of the frontal association areas, either partial or complete, resulted in different effects on the two types of tests.

(a) Memory for simple problem box habits and for visual discrimination habits was not impaired, nor was the ability to learn new tasks of a similar nature reduced.

(b) The ability to perform delayed response was abolished by complete lesions of the frontal areas. The subjects failed in this test with delays as short as one or two seconds.

(c) Subtotal lesions caused a shortening of the time through

require for their solution not only present sensory items but also elements of past experience which can be introduced only through the action of memory. In the visual discrimination and puzzle box experiments the differential cues determining whether the animal shall go to the left or right box on a given trial, or whether it shall pull a rope projecting from the side of the problem box or turn a crank, are inherent in the test situation at the time of response. It is clear that the frontal areas are not concerned with retention and activation of stable habits of this type. But in the delayed response test and in the instrumentation tests in which all items are not available in the visual field, the cues determining which of two cups shall be raised, or where a stick shall be secured for use in drawing in the food, if indeed it is to be sought at all, are carefully eliminated from the situation. In some manner the differential cues must be supplied by the subject from its past experience, namely observation of the experimenter concealing the food or placing the stick out of the immediate field of the problem. Kohler's description of the efforts of the chimpanzee Sultan to secure a suspended banana illustrates well our point. Several attempts to reach the lure with objects in the immediate vicinity had failed when

*"quite abruptly, and without visible external cause, Sultan ceased belabouring door and bolt (with which he had been attempting to reach the lure), remained motionless, sprang to the ground, traversed the passage at a gallop, and was back in a moment with the box (which he had been shown at the beginning of the experiment). In that second, in which his behavior obviously took a fresh direction, the door covered and concealed the objective from his view which did not prevent him from trying to tear away the bolt as an implement: yet the box was at a much more considerable distance, around the corridor corner, and behind his back. It is evident, however, how immensely delayed the solution may become when the implement can be introduced only through the action of memory" (33, p. 52).*

This then appears to be the peculiar contribution of the frontal association areas, namely, recall of a particular past event which may be only in mediate association with some aspect of the present

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